PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant(s): Yang, et al.

Application: 10/074,272

Filed: February 14, 2002

Confirmation No: 4926

For: THIN FILM WITH NON-SELF-AGGREGATING UNIFORM HETERO-GENEITY AND DRUG DELIVERY SYSTEMS MADE THEREFROM

Examiner: Chan, Sing P.

Group Art Unit: 1734

Docket: 1199-4 RCE

Date: March 12, 2007

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RESPONSE TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF PURSUANT TO 37 C.F.R. §41.37

Sir:

This paper is being filed in response to a Notification of Non-Compliant Appeal Brief Pursuant to 37 C.F.R. §41.37 dated February 13, 2007 in the above-identified application, a response to which is due March 15, 2007.

REMARKS

Appellants have been notified that the Appeal Brief filed on September 26, 2006 fails to comply with 37 C.F.R. §41.37. More specifically, the Notification of Non-Compliant Appeal Brief indicates that the Appeal Brief did not contain a statement of the status of all claims filed in the application. In particular, the Appeal Brief did not indicate that claims 1-53, 56-61, 79, 82, 92, 105, 107, 113, 115 and 118 have been cancelled.

In response to this Notification of Non-Compliant Appeal Brief, Appellants submit herewith an amended Appeal Brief, which contains a statement of the status of all claims filed in the application. Entry of this Appeal Brief is respectfully requested.

It is submitted that no additional fee is occasioned by this response. However, if any fees are required in connection with this Appeal, please charge any such additional fees to Deposit Account No. 08-2461.

Respectfully submitted,

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APPEAL BRIEF AND RESPONSE TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF

Sir:

Appellants resubmit this amended Appeal Brief (originally submitted on September 26, 2006) in response to the Notification of Non-Compliant Appeal Brief dated February 13, 2007.

Appellants have appealed the Final Rejection of claims 91, 93-104, 106, 108-112, 114, 116, 117 and 119 from the Office Action dated January 20, 2006 in the above-identified application. Appellants timely filed a Notice of Appeal on June 20, 2006. This Notice of Appeal was received at the U.S. Patent and Trademark Office on June 26, 2006. Therefore, the due date for filing a Brief in support of the appeal is September 26, 2006 with a one-month extension of time, a petition for which is concurrently submitted herewith.

As required by 37 C.F.R. §41.37, a single copy of this brief is being filed with the filing fee of $250.00 for a small entity. Please charge the fee to Deposit Account No. 08-2461. Kindly charge or credit any fees or overpayments, respectively, to Deposit Account No. 08-2461.

1. REAL PARTY IN INTEREST

The real party in interest in the present appeal is MonoSolRx, LLC, a company registered in the state of Delaware, having acquired rights by way of assignments recorded in the United States Patent and Trademark Office at Reel 013002, Frame 0285 and Reel 014315, Frame 0613.

2. RELATED APPEALS AND INTERFERENCES

No related appeals or interferences are known to Appellants or Appellants' legal representative which will directly affect or be directly affected by or have bearing on the Board's decision in this appeal.

3. STATUS OF THE CLAIMS

Claims 54, 55, 62-78, 80, 81, 83-91, 93-104, 106, 108-112, 114, 116, 117 and 119 are in the application. Claims 1-53, 56-61, 79, 82, 92, 105, 107, 113, 115 and 118 have been cancelled.

Claims 91, 93-104, 106, 108-112, 114, 116, 117 and 119 are finally rejected and on appeal.

Claims 54, 55, 62-78, 80, 81 and 83-90 are presently withdrawn and not on appeal.

No claims presently stand allowed.

4. STATUS OF AMENDMENTS

The final Office Action of January 20, 2006 included, *inter alia*, a rejection of claims 91-104, 106, 108-112, 114, 116, 117 and 119 under 35 U.S.C. §112, second paragraph, as allegedly

being indefinite. On May 9, 2006, Appellants' filed a Response to the final Office Action with amendments to claims 91, 101, 104, 106, 108, 110-112, 114, 116, 117 and 119 directed to overcoming at least the rejection under 35 U.S.C. §112, second paragraph. In an Advisory Action dated May 22, 2006, the Examiner indicated that these amendments were entered for purposes of Appeal. In view thereof, it is Appellants' understanding that the 35 U.S.C. §112, second paragraph rejection has been overcome.[1] These amendments have been incorporated into the claims appearing in the Claims Appendix submitted herewith.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The presently claimed invention is directed to a process for making a self-supporting and edible film having a substantially uniform distribution of components. The self supporting, edible film is particularly useful for delivery of pharmaceutical actives. The process for making the edible film is designed to maintain the compositional uniformity of components distributed throughout the film, which is particularly necessary when actives, such as pharmaceutical actives, are incorporated into the film. In the pharmaceutical context, it is essential that the edible film is compositionally uniform so that it can be divided into individual film dosage units, each dosage unit having the appropriate amount of active when swallowed, such that regulatory approval can be secured. (p.5, ¶13).

As seen in independent claims 91, 101, 104, 106, 108, 110, 111, 112, 114, 116, 117 and 119, the self-supporting edible film is generally prepared by the initial steps of providing, combining and/or mixing an edible water-soluble polymer component, water and an active component to form an edible matrix with a uniform distribution of components; deaerating the matrix by mixing; and forming a wet film from the deaerated matrix. (p.5, ¶14; p.12, ¶42; claim 101, steps (a)- (c)).

[1] If Appellants' understanding with respect to the rejection under 35 U.S.C. §112, second paragraph, is incorrect, Appellants respectfully request an opportunity to address the rejection in a further submission to the Board.

Thereafter, the edible film is further prepared by rapidly forming a visco-elastic film by applying hot air currents to the film to prevent flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining compositional uniform distribution of components in the film; and further drying the visco-elastic film to form a self-supporting edible film. (p.5, ¶14; pp.8-9, ¶24; p.28, ¶105; claim 101, step (d)).

Desirably, as recited in claims 91, 108, 112, 117 and 119, the hot air currents are applied to the bottom of the film, with substantially no top air flow. (p.6, ¶15; p.11, ¶38). This allows the depth of the film to be dried prior to forming a polymer skin on the top surface of the film, as recited in claim 106, which would disrupt the surface of the film, leading to non-uniformity. (p.11, ¶38). The dried, self-supporting film is uniform in the distribution of the components contained therein, weight and thickness, as recited in claim 104. (p.11, ¶36; pp.40-41, ¶153).

With respect to claim 91, the film first may be fed onto the top side of a surface prior to the application of hot air currents. The hot air currents then are applied to the bottom side of the surface with substantially no top air flow. (p.6, ¶15).

Dependent claim 95 specifically requires that the wet film formed from the deaerated matrix have a thickness of at least about 500μm. (p.29, ¶110).

With respect to claim 101, the process may further include a step of dividing the dried film into individual dosage units of equal dimensions and compositional make-up. (p.5, ¶13; pp.40-41, ¶153).

With respect to claim 106, the wet film is formed from the deaerated matrix within a time period before the active contained therein degrades. (p.13, ¶43).

With respect to claim 108, the hot air currents may be applied to the bottom surface of the film at a higher velocity than to the top surface of the film during drying. (Examples, Table 7).

With respect to claim 110, the hot air currents applied to dry the film are less than that which would cause surface rippling or skinning. (p.11, ¶38). This permits the film to sufficiently thicken in viscosity to lock-in volumetric uniformity while permitting evaporation of water through the non-skinned surface.

With respect to claim 111, the top surface of the dried film is non-rippled. (p.11, ¶38).

With respect to claim 112, the deaeration step further includes a vacuum to deaerate the film matrix. (p.5, ¶14).

With respect to claim 114, the hot air currents applied to dry the film are insufficient to cause one or more of: surface skinning, surface rippling, self-aggregation of components, non-uniformity in film thickness and non-uniformity in mass per unit volume of the film. (p.11, ¶38; p.12, ¶39; p.33, ¶122).

With respect to claim 116, the process may further include a step of adding an anti-foaming agent to the matrix to release oxygen therefrom prior to deaerating the matrix by mixing. (p.22, ¶78).

With respect to claim 117, the process may further include the preliminary steps of forming a masterbatch premix of an edible water-soluble polymer and water; deaerating the premix by mixing; feeding a predetermining amount of the deaerated premix to at least one mixer; adding an active component to the mixer; and mixing the components to achieve a uniform distribution thereof. Thereafter, the wet film is formed and dried as discussed above. (p.13, ¶¶43-44; Fig. 6).

With respect to claim 119, heat is applied to the bottom side of the surface onto which the film is fed for the drying step. (p.28, ¶105).

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following grounds of rejection are to be reviewed on this Appeal:[2]

1. Claims 91, 93, 97, 100, 101, 106, 108, 109, 111, 112, 114, 117 and 119 have been rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,660,292 to Zerbe et al. (hereinafter "Zerbe") in view of U.S. Patent No. 5,881,476 to Strobush et al. (hereinafter "Strobush") and U.S. Patent No. 5,044,761 to Yuhki et al. (hereinafter "Yuhki").

2. Claims 94 and 95 have been rejected under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and U.S. Patent No. 5,629,003 to Horstmann et al. (hereinafter "Horstmann").

3. Claim 96 has been rejected under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and U.S. Patent No. 4,478,658 to Wittwer (hereinafter "Wittwer").

4. Claims 98, 99, 102 and 103 have been rejected under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and U.S. Patent No. 6,231,957 to Zerbe et al. (hereinafter "Zerbe '957").

5. Claims 104 and 110 have been rejected under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and Horstmann.

6. Claim 116 has been rejected under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and U.S. Patent No. 5,733,575 to Mehra et al. (hereinafter "Mehra").

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[2] In addition to the grounds of rejection delineated in this section, the final Office Action dated January 20, 2006 also included an obviousness-type double patenting rejection of claim 119 over claim 1 of Appellants' co-pending Application No. 10/768,809 in view of U.S. Patent No. 5,044,761 to Yuhki et al. As this is a provisional obviousness-type double patenting rejection, it is not being addressed on appeal.

7. ARGUMENTS

A. CLAIMS 91, 93, 97, 100, 101, 106, 108, 109, 111, 112, 114, 117 AND 119 ARE PATENTABLE OVER ZERBE IN VIEW OF STROBUSH AND YUHKI

The Examiner has rejected claims 91, 93, 97, 100, 101, 106, 108, 109, 111, 112, 114, 117 and 119 under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush and Yuhki. As set forth in the final Office Action dated January 20, 2006, the Examiner asserted that Zerbe discloses a method of forming flavored film. According to the Examiner, the method of Zerbe includes providing a polymer component, flavoring and other ingredients in water for forming a solution, coating the solution, or matrix, onto a carrier substrate, drying the film with hot air and removing the film after drying. The Examiner admitted, however, that Zerbe fails to disclose deaerating the matrix by mixing, applying hot air to the bottom of the substrate with substantially no top air flow to dry the film and rapidly form a viscoelastic film, and drying the film in a manner that prevents air flow migration and intermolecular forces from forming aggregates or conglomerates to maintain compositional uniformity. The Examiner relied upon Strobush and Yuhki for allegedly overcoming these deficiencies.

In particular, in the final Office Action, the Examiner asserted that:

> . . . directing hot air to the bottom of the substrate with a higher air current at the bottom than the top or substantially no top air flow to dry the film is well known and conventional as shown for example by Strobush et al.

(Office Action, at page 6).

More specifically, the Examiner asserted that Strobush teaches a method for drying a coating on a substrate including the steps of providing a substrate with a coating applied thereto and feeding the coated substrate into a drying apparatus. The Examiner correctly pointed out that Strobush's drying apparatus includes air foils located below the coated substrate that direct

drying gas to the bottom surface of the substrate, as well as top air bars to supply top-side air to dry the coated substrate "without mottle defects." However, the Examiner was incorrect in stating that "mottle" is defined as "uniform thickness or uniform density, which is without forming aggregates or conglomerates with uniform distribution of components." (Office Action, at page 6) (citations omitted). In fact, the Examiner has ignored Strobush's definition of mottle. In particular, Strobush defines "mottle" as "an undesirable surface defect because it detracts from the appearance of the finished product." (Strobush; Col. 2, lines 6-19). As can be seen therefrom, mottle is actually a surface defect, not a uniformity defect throughout the thickness of a film. Mottle and unit volume compositional uniformity (content uniformity) are entirely different and unrelated.

Nevertheless, based on these assertions and assumptions, the Examiner concluded that it would have been obvious to one of ordinary skill in the art to:

> . . . dry the coating on a substrate by directing drying gas to the bottom of the coated substrate as disclosed by Strobush et al in the method of Zerbe et al ('292) to dry the coating on a substrate without mottle and at higher web speeds.

Acknowledging that this alleged combination of references still failed to disclose deaerating the mixture by mixing, the Examiner further relied upon Yuhki to overcome this additional deficiency. Specifically, the Examiner asserted that Yuhki discloses a method of dissolving and deaerating a powder material. According to the Examiner, it would have been obvious to one skilled in the art to slowly stir the liquid and powder mixture to deaerate the mixture as disclosed by Yuhki in the method of Zerbe as modified by Strobush "to dissolve powder material and to deaerated [sic] rapidly and easily with no bubbles being developed." (Office Action, at page 7).

Zerbe, Strobush and Yuhki, however, do not together form a proper rejection of claims 91, 93, 97, 100, 101, 106, 108, 109, 111, 112, 114, 117 and 119 for at least the following

reasons. First, Strobush is nonanalogous art and is not properly useable in formulating a rejection of the claims herein. Second, there is no motivation to combine Zerbe and Strobush as suggested by the Examiner. Third, Strobush teaches away from Appellants' claimed invention. Fourth, there is no reasonable expectation of success. Accordingly, there is no *prima facie* showing of obviousness based on this hypothetical combination.

Furthermore, even assuming *arguendo* that a hypothetical combination of Zerbe, Strobush and Yuhki can somehow be made, the hypothetical combination fails to suggest combining all of the process limitations of Appellants' claims, particularly claim 117. Thus, the rejection of claim 117 based on Zerbe, Strobush and Yuhki should also be withdrawn on this ground.

1. **Strobush is Nonanalogous Art**

The presently claimed invention is directed to overcoming problems in forming edible film strips for individual dosing of actives, particularly drugs, which are safe and effective for human consumption. In stark contrast, Strobush relates to an apparatus and method for producing a high-quality photographic or thermographic image. Strobush bears no relevance on the pharmaceutical field of art, nor the present inventors' concerns in achieving safe and effective film dosage forms. It simply does not make any sense in reality to apply a photographic imaging reference to an invention on edible products intended as a pharmaceutical delivery system.

By definition, if a reference is "nonanalogous art," it cannot be relied upon as a basis for rejecting an applicant's claims. As set forth in the case law, there are two criteria for determining whether or not a prior art reference is "analogous":

> (1) whether the art is from the same field of endeavor, regardless of the problem addressed, and (2) if the reference is not within the field of the inventor's endeavor, whether the reference still is

> reasonably pertinent to the particular problem with which the inventor is involved.

In re Clay, 966 F.2d 656, 658-59, 23 U.S.P.Q.2d 1058, 1060-61 (Fed. Cir. 1992); *see also In re Oetiker*, 977 F.2d 1443, 1447, 24 U.S.P.Q.2d 1443, 1445 (Fed. Cir. 1992); *In re Deminski*, 796 F.2d 436, 442, 230 U.S.P.Q. 313, 315 (Fed. Cir. 1986).

A reference is only "reasonably pertinent" if it is one which "logically would have commended itself to an inventor's attention in considering his problem." *In re Clay*, 966 F.2d at 659.

As the court further explained in *In re Oetiker*:

> Patent examination is necessarily conducted by hindsight, with complete knowledge of the applicant's invention, and the courts have recognized the subjective aspects of determining whether an inventor would reasonably be motivated to go to the field in which the examiner found the reference, in order to solve the problem confronting the inventor. We have reminded ourselves and the PTO that it is necessary to consider 'the reality of the circumstances' - in other words, common sense - in deciding in which fields a person of ordinary skill would reasonably be expected to look for a solution to the problem facing the inventor.

In re Oetiker, 977 F.2d at 1447 (citations omitted).

In accordance therewith, MPEP §2141.01(a) similarly expresses the standard that only references that relate to the field of an inventor's endeavor or that are reasonably pertinent to the particular problem to which an inventor is concerned with may be relied upon in formulating a rejection.

Strobush is outside the inventors' field of endeavor and is not at all concerned with the particular problems with which the inventors herein were concerned. Strobush relates only to the

problem of preventing mottle in highly **volatile organic solvent**-based coatings used to form photographic or thermophotographic film, which is an entirely different and unrelated problem than the problems addressed by the present invention, as described herein and further indicated in the Declaration Under 37 C.F.R. §1.132 by Dr. Rhyta Rounds submitted with Appellants' Response dated May 9, 2006, a copy of which is attached hereto as Appendix 1 (hereinafter the "Rounds Declaration").

a. APPELLANTS' PROBLEM was to obtain compositional uniformity throughout film suitable for human consumption whereas STROBUSH'S PROBLEM was to reduce surface defects (mottle) in a finished photographic product

As indicated in the specification of the present application, the inventors were concerned with forming self supporting, edible films that can be divided into equally sized dosage units having substantially equal amounts of each compositional component present. (Application; p.4, ¶10). The dosage units include a significant component, i.e., a drug or other active as defined in the specification. Hereinafter, the significant component will be referred to as "Active". The inventors were particularly concerned with forming ingestible films for use as pharmaceutical dosage delivery systems in which each dosage unit, e.g., each individual dosage film unit, contains the proper amount of Active. (Application; p.4, ¶10). As further explained in the specification, the prior art has been unsuccessful in providing individual film dosage units containing the proper amount of Active, which is necessary for satisfying federal regulatory requirements for making a commercial product. (Application; p.2, ¶4).

Specifically, as stated in the application:

> Currently, by law, dosage forms may not vary more than 10% in the amount of active present. When applied to dosage units based on films, this virtually mandates that uniformity in the film be present.

(Application; p.2, ¶6).

As further supported by Dr. Rounds:

> Compositional Uniformity is vital for oral film delivery strips to provide safe and effective consumer products. Without Compositional Uniformity, individual film products containing drug cannot achieve FDA approval for consumer use and essentially have no value.

(App. 1; Rounds Declaration, ¶30).

For example, a dosage unit of film that is labeled 30mg of drug can only vary from 27mg to 33mg according to FDA law. To satisfy this requirement, each unit volume of the film must be compositionally uniform, such that when consumed it delivers the proper Active amount. Volume is a three-dimensional consideration, as opposed to surface defects such as those in Strobush, which are merely a two-dimensional concern.

The problem of providing compositionally uniform films for use as oral dosage units, with which the subject inventors were concerned, involves solving a number of different technical problems, none of which relate to mottle. As indicated in the Rounds Declaration, achieving such uniform film products involves overcoming a variety of technical difficulties due to the relatively large size of Active particles, the irregular shape of Active particles, the ability to maintain the particles in dispersion without settling out, the use of <u>aqueous-based systems</u>, the relatively thick films, and external forces, among others. (App. 1; Rounds Declaration, ¶¶ 19-20, 23-25). Random air voids, Active (e.g. drug) component particle migration and Active component particle aggregation are just some of the resultant problems commonly experienced in such systems. (App. 1; Rounds Declaration, ¶ 25). As asserted by Dr. Rounds, overcoming such problems to obtain compositionally uniform products is "critical for drug-containing films in order to provide safe and effective consumer products and thereby satisfy FDA-approval requirements." (App. 1; Rounds Declaration, ¶¶ 18, 30).

b. STROBUSH'S PROBLEM was to reduce surface defects (mottle) in a finished photographic product

In contrast, Strobush is directed to an apparatus and method for producing non-ingestible photothermographic, thermographic and photographic coatings on a permanent, synthetic organic polymer substrate without mottle. (Strobush; col. 2, lines 8-15). Strobush has nothing to do with consumable products at all, nor the concerns involved in obtaining regulatory approval for consumable products. Rather, mottle is the sole problem addressed by Strobush. As set forth in the Rounds Declaration, Strobush is concerned with surface defects of the permanently coated substrate because they would detract from the appearance of the finished product, e.g. a photograph. (App. 1; Rounds Declaration, ¶¶ 10-11, 17). Strobush even specifically defines "mottle" as "an undesirable defect because it detracts from the appearance of the finished product." (Strobush; Col. 2, lines 6-19).

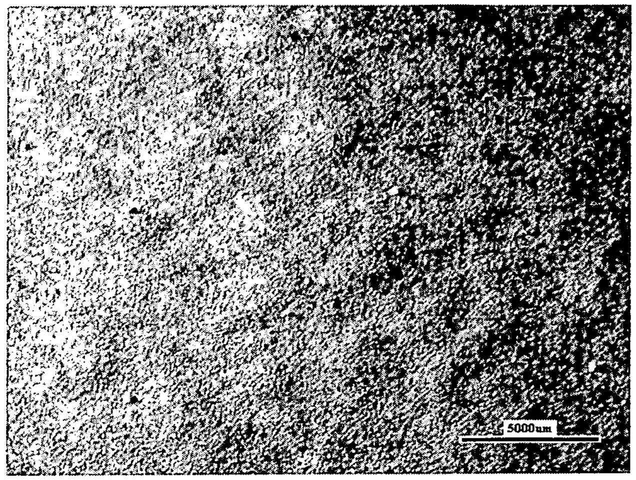
Mottle is a serious problem in Strobush because its thin (sub-millimeter) coatings are emulsion systems composed of very small silver particles dissolved in highly volatile non-aqueous solvents. (App. 1; Rounds Declaration, ¶¶ 12-14). Such problem is addressed by using a complex drying apparatus, which includes a sequence of zones, to control the factors leading to mottle. (App. 1; Rounds Declaration, ¶¶ 15-16). The apparatus used in preparing the coated substrates of Strobush involves very different chemical systems and criteria than the systems and objectives sought by the inventors herein. (App. 1; Rounds Declaration, ¶¶ 21-26). A table from the Rounds Declaration illustrating a number of the contradictory features is set forth below:

Inventive Process Characteristics	Strobush Process Characteristics
Edible film	Photographic coating
Water	**MEK (highly volatile toxic organic solvents)**
Viscoelastic matrix	Low viscosity (rheology not mentioned)
Active (e.g., temperature-, oxidative- and/or hydrolytically-sensitive)	No ingestible actives
Relatively large particles (macro-suspension)	Nanoparticles (colloidal dispersion)
Self supporting doses	Permanent thin coating on a substrate
Rapid heating to create large temperature differential	**Very small temperature differential in a plurality of heating zones**
Benard cells	No Benard cells
De-aeration	De-aeration not possible
Compositional uniformity (mass of active/unit volume)	Mottle free (perfect surface)
Surface imperfections generated (mottle is acceptable)	No surface imperfections

(App.1; Rounds Declaration, ¶27) (emphasis added).

As can be seen from the distinctly different systems and concerns illustrated above, there is nothing in Strobush that would have "logically commended itself" to the present inventors' attention or anyone skilled in the art of pharmaceutical dosage forms.

It is clear, therefore, that the inventors herein seeking to satisfy the problems associated with ingestible film dosage units would not look to Strobush. As discussed above, Strobush is merely concerned with the <u>surface appearance</u> of a permanently coated substrate used in making <u>non-ingestible</u> imaging articles -- properties which play no part in solving the technical problems of the present invention. Indeed, as stated in the declaration, "surface imperfections in the inventive films are expected." (App. 1; Rounds Declaration, ¶ 25). The following photograph, which was shown during the Examiner Interview on May 3, 2006, illustrates that the uniform films produced by the presently claimed process often exhibit surface irregularities, including mottle.



Compositionally uniform inventive
film (top view, 5000μm)
(with surface mottle)

Hence, solving the problem of surface mottle would not achieve compositional uniformity in active-containing films for human consumption. (App. 1; Rounds Declaration, ¶22). Contrary to the Examiner's assertions, therefore, mottle is wholly unrelated to the problem of achieving compositionally uniform film dosage units for oral administration of actives. (App. 1; Rounds Declaration, ¶¶ 21-26).

Therefore, not only is Strobush not in the field of the inventors' endeavor, Strobush is not at all relevant to the problem with which the present inventors were concerned. In considering the inventors' specific problem of providing ingestible films that can be divided into equally sized dosage units having substantially equal amounts of each compositional component present, particularly the Active, one skilled in the art would not look to Strobush. For all the reasons stated above, Strobush is <u>not</u> analogous art and can not be properly relied upon in formulating any rejection herein.

2. **No Motivation to Combine Zerbe, Strobush and Yuhki**

As set forth in MPEP §2143.01, "Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art."

As the court further explained in *In re Paulsen*:

> . . . we have been guided by the well settled principles that the claimed invention must be considered as a whole, multiple cited prior art references must suggest the desirability of being combined, and the references must be viewed without the benefit of hindsight afforded by the disclosure.

In re Paulsen, 30 F.3d 1475, 1482, 31 U.S.P.Q.2d 1671, 1676 (Fed. Cir. 1994).

a. **Zerbe and Strobush are directed to divergent teachings**

Contrary to the Examiner's assertions, there is no motivation to combine Zerbe and Strobush. Zerbe relates to rapidly disintegrating flavored films. The films are used to flavor food items, such as hamburgers or pizza. The films include a mixture of hydroxypropyl cellulose and modified starch, and a flavor ingredient. Zerbe only generally mentions drying the films and uses conventional hot air ovens to do so. Zerbe does not suggest that any concerns are raised by such conventional drying and based on his disclosure, one of ordinary skill in the art would assume there are no problems to be overcome. In fact, Zerbe discusses drying as if it is merely incidental to his invention and can be accomplished without overcoming any technical problems whatsoever. Therefore, Zerbe provides no reason or suggestion to look to any other art for a different method of drying its film products. Zerbe teaches the skilled artisan that conventional oven drying is sufficient to dry films.

In contrast, Strobush, as discussed above, has nothing to do with edible products. Rather, Strobush is directed to non-ingestible coated substrates used in producing imaging articles.

Strobush's coatings are not self-supporting films, but are permanent coatings that overlay images, such as photographs. Strobush's systems contain small silver particles dissolved in volatile, toxic non-aqueous solvents that evaporate rapidly. Such rapid evaporation can lead to surface defects in Strobush's systems. This is an entirely different technical field of endeavor from the formation of edible film products, such as Zerbe's films, involving completely different chemistry and processing considerations. (App. 1; Rounds Declaration, ¶¶ 21-26). There would be no motivation for one of ordinary skill in Zerbe's field of art to look to such a wholly unrelated technical area for processing edible films.

Moreover, the purpose of Strobush is to reduce mottle, or surface defects in the appearance of the coated substrate. Surface appearance, however, is not typically a problem in edible film products. (App. 1; Rounds Declaration, ¶25). As such, there additionally would be no motivation for one skilled in Zerbe's field of art to look to Strobush because the primary objective of Strobush is not germane to edible film processing. The Examiner's alleged motivation to combine Strobush and Zerbe, i.e., to produce Zerbe's films without mottle, therefore is improper.

Therefore, there is no suggestion in Zerbe itself to look to any other art, particularly unrelated art such as Strobush, for methods of drying its edible film products. Moreover, there would be no motivation from one skilled in the art's general knowledge to look to such an unrelated area of technology for processes useful in forming edible film products. Further, even if Zerbe and Strobush were properly combinable, attempting to achieve a mottle-free surface would not provide an edible active-containing film that is compositionally uniform throughout. It is respectfully submitted that no motivation is present to combine Zerbe and Strobush as suggested by the Examiner. Rather, the Examiner's combination of Zerbe and Strobush improperly relies on hindsight afforded by Appellants' disclosure. *See In re Paulsen*, 30 F.3d at 1482.

b. Strobush and Yuhki also are directed to divergent teachings

Furthermore, there also would be no motivation to combine the teachings of Strobush with Yuhki. More specifically, Appellants' present claims also require a deaeration by mixing step, during which gas is removed from the film composition mixture. This step assists in obtaining uniformity in the film composition by preventing voids therein. The Examiner cited Yuhki for its alleged disclosure of a deaeration step. Specifically, Yuhki deaerates concentrated water-based solutions of powdered materials. Yuhki's deaeration process involves reducing the pressure in the tank in which the liquid is housed, agitating the liquid at high speed and cycling through further decompression steps while continuously agitating the liquid. Such a deaeration process, however, would be contrary to the teachings of Strobush because it would rapidly remove the volatile organic solvent and defeat Strobush's purpose of slow, incremental drying of the coated substrate. In particular, rapid evaporation of air would cause turbulence in Strobush's systems and the silver particles on the surface would become disturbed. This is contrary to Strobush's whole purpose. As Strobush requires highly volatile organic solvents, it is not clear how Yuhki, which is an aqueous system, is applicable. In addition, Yuhki's deaeration process may create a dangerous, explosive situation in Strobush's systems. The teachings of Yuhki with respect to deaeration, therefore, are contrary to Strobush. Such divergent teachings are not properly combinable.

In view thereof, the prior art fails to suggest the desirability of combining the divergent teachings of Zerbe, Strobush and Yuhki, and thus, no *prima facie* showing of obviousness has been made.

3. Strobush Teaches Away From Water-Based Ingestible Self-Supporting Films

"A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." MPEP §2141.02.

When considered as a whole, the disclosure of Strobush is distinctly different from and even teaches away from the presently claimed invention. The differences between Appellants' claimed process and Strobush go well beyond the fact that they are entirely different technologies. Specifically, Strobush is directed to a specialty apparatus designed to make permanent coatings on an image substrate. (Strobush; Col. 9, lines 5-6). This is in contrast to the self-supporting, edible films of the present invention. The inventive process and the conditions required by the Strobush apparatus, as well as their respective end-products, are diametrically opposed in many respects. (App. 1; Rounds Declaration, ¶¶ 27-28) (providing a table in which many of the differences are juxtaposed).

a. <u>It is improper to select only bottom drying element from Strobush's complicated drying disclosure</u>

Although Strobush mentions application of heat to the bottom of the coated substrate to dry and permanently attach the photographic emulsion layers thereto, this disclosure is part of a complicated drying apparatus with multiple zones and sub zones. Strobush's complicated drying apparatus is directed to the purpose of very slowly removing organic solvent without causing the silver particles in the coating to be disrupted, which would result in a mottled surface. Using this specially designed drying apparatus, Strobush incrementally controls the temperature differential between his single monolayer of silver particles and the drying environment. By minimizing the $h\Delta T$ in these zones, Strobush is able to very slowly remove the highly volatile organic solvent (2-butanone, also known as MEK), with a minimum disturbance of the silver particles. Strobush's goal is to align the silver particles as flat and evenly as possible on the surface of the photographic paper such that when the photographic film is exposed to light and developed, surface defects in the image, i.e., mottle, is minimized. Rather than ramping up the temperature quickly, as in the present invention, Strobush does the opposite. In fact, Strobush uses a drying apparatus which is about 100 feet long (30 meters) to slowly dry. (Strobush; Col. 13, line 62).

Strobush does not simply use bottom drying. The Strobush apparatus uses it along with top air and ventilation systems to remove the volatile, toxic fumes from the multiple heating

zones. The thrust of Strobush is the incremental temperature differential between the many zones. In figure 20, for instance, Strobush indicates the presence of 15 zones (drying gas temperatures) where the temperature differential is minimized to keep down mottle formation.

Moreover, Strobush is drying a colloidal dispersion of very fine silver particles in MEK. Such a dispersion behaves very differently than suspensions of macroparticles in an aqueous system, such as those of the present invention. (App. 1; Rounds Declaration, ¶ 25). Strobush's teachings are not in any way comparable to the presently claimed invention and in fact contrary to the invention. Whereas the present invention claims rapidly forming a visco-elastic film to lock-in uniformity, Strobush teaches to very slowly change the temperature through a series of zones and is completely silent as to rheology or the formation of a visco-elastic film.

Additionally, Strobush seeks to eliminate photographic surface defects (mottle) by reducing turbulence in its coatings during drying. Turbulence is diminished by Strobush's very slow and incremental heating and controlled pressure and temperature incrementals throughout its series of drying zones. Strobush uses a low energy approach to highly control the drying rate. In contrast, Appellants' rapid drying aims to encourage turbulence in its film compositions to ensure mixing and compositional uniformity throughout. The presently claimed invention uses a high energy approach to drying. This distinction in drying approaches between Strobush and the presently claimed invention is a difference-in-kind. Simply stated, Appellants' rapid bottom heating causes a different phenomenon to take place.

Thus, taking only the bottom drying disclosure from Strobush and applying it to a totally different type of technology, i.e., a water-based, edible film, is picking and choosing an element from the reference without giving consideration to its full teachings. In essence, the Examiner's assertions have divorced Strobush's process from his complicated apparatus. Neither bottom drying nor any of Strobush's process steps can be separated from his apparatus, which requires multi-zoned and sub-zone heating areas that are required to slowly evaporate the solvent to leave behind surface-aligned silver particles. It is improper to select only this aspect from a

complicated apparatus for drying coated substrates, thereby ignoring the teachings of the reference as a whole. *See In re Wesslau*, 353 F.2d 238, 241, 147 U.S.P.Q. 391, 393 (C.C.P.A. 1965) (explaining that "it is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art"); MPEP §2141.01.

b. <u>Strobush involves highly volatile organic systems and TEACHES AWAY from water-based systems</u>

Moreover, considering the reference in its entirety, Strobush teaches away from using its apparatus to dry water-based systems. The only references to water in Strobush appear in its discussion of prior art. (Strobush; Col. 3, line 59 and Col. 4, line 1). Strobush explains that drying water-based latex paint coatings solves an entirely different problem from mottle. (Strobush; Col. 3, line 58 to Col. 4, line 8). Strobush further asserts that the problems encountered in drying permanent coatings of water-based paint are not relevant to his process. (Strobush; Col. 4, lines 6-8). As explained by Dr. Rounds, "Strobush itself recognizes that mottle is a different problem from other surface defects in aqueous systems." (App. 1; Rounds Declaration, ¶26). Thus, the disclosure of Strobush leads away from the applicability of its drying apparatus to water-based systems. A process for forming self-supporting, edible water-based films would clearly be even further from Strobush.

Although the Examiner alleged that Strobush may be applied to other types of coatings, there is absolutely no suggestion to apply its apparatus to water-based coatings. Specifically, during an Examiner Interview, the Examiner raised the following statement in Strobush:

> While suitable for a wide variety of coatings, the drying apparatus 10 is particularly suited for drying photothermographic and thermographic coatings to prepare photothermographic and thermographic articles.
>
> (Column 9, lines 9-12).

As discussed above, the only mention of water in Strobush is in the discussion of prior art, in which Strobush distinguishes the problems of prior art water-based systems from his organic solvent-based systems. In actuality, it would be impossible to make the photographic or thermographic image end-product of Strobush in an aqueous system. More specifically, as seen in Strobush, if too much heat is transferred to the coated substrate for any given distance, then the coated substrate mottles. For example, as seen in Table 5 of Strobush, Example 1-3, which had a high heat transfer rate (hΔT) of 532 cal/m^2 s, exhibited high mottle as compared to Examples 1-1 and 1-2, which had significantly lower heat transfer rates. Similarly, as seen in Strobush's Table 6, Example 2-3 had a high heat transfer rate (837 cal/m^2 s) and exhibited high mottle as compared to Examples 2-1 and 2-2. Also, in Strobush's Table 8, Example 4-1 had a high heat transfer rate (1770 cal/m^2 s) and exhibited high mottle as compared to Examples 4-2 and 4-3. For this reason, Strobush must keep the heat transfer rate to the coated substrate below a certain level to reduce mottle.

In accordance therewith, Strobush specifically states that:

> **The heat transfer rate to the coating 12 is the key to preventing or minimizing mottle formation.**[] In order to prevent mottle formation in the coating 12 during drying, this heat transfer rate (hΔT) to the coating 12 must be kept below a threshold mottle-causing value.

(Strobush; Col. 12, lines 40-44) (emphasis added).

As seen in Figs. 19 and 21 of Strobush, therefore, the temperature of the drying gas is increased very slowly over a long distance in Strobush's drying apparatus. For instance, the temperature of the drying gas does not reach 100°C until the coated substrate has traveled about 17m (over 51 feet) through the apparatus. This slow temperature increase over a long distance provides a low heat transfer rate to the coated substrate, and thus, according to Strobush, is the key to preventing mottle.

In contrast, much higher heat transfer rates are required to remove water from aqueous-based systems than volatile organic solvents from Strobush's organic solvent-based systems, i.e., a greater amount of energy (heat) is required to evaporate a given amount of water as compared to MEK. Additionally, as the aqueous films of the present invention dry, even greater amounts of energy are required to drive off additional water from the viscoelastic matrix that is formed. For instance, the present application discloses rapid and high temperature increases over short drying distances to remove the water from its film. (Application; p.28, ¶105; p.37, Table 7 and ¶137; p.40, ¶149). Greater heat differentials in a short period of time (e.g., up to 4 minutes, p.28, ¶105 of the Application) would cause turbulence in Strobush's systems. Such high heat transfer rates necessary for the removal of water would lead to mottle in Strobush's systems and go against the primary teachings of Strobush. Hence, it would not be possible to make Strobush's finished products in an aqueous-based system. They must be made in a volatile organic system.

In citing the above passage and suggesting Strobush's applicability to aqueous-based systems, the Examiner may have overlooked the importance of the heat transfer rate ($h\Delta T$) in Strobush, as demonstrated by the Examples and figures discussed above. Thus, a fair reading of the statement in the above passage cannot be that one could switch to a water-based system. *See Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448, 230 U.S.P.Q. 416, 419-20 (Fed. Cir. 1986) (holding that a single line should not be taken out of context to show obviousness, but rather, a reference should be considered in its entirety).

Furthermore, Strobush subsequently explains that materials suitable for drying in its apparatus include "[a]ny mottle-susceptible material, such as graphic arts materials and magnetic media." (Strobush; Col. 16, lines 62-63). As mentioned above, mottle is not the concern in drying edible, self-supporting films. (App. 1; Rounds Declaration, ¶ 25). Accordingly, upon a proper consideration of Strobush as a whole, there is no suggestion and even a teaching away from applying its complex apparatus to the preparation of edible, self-supporting water-based films.

It is, therefore, relevant that Zerbe requires water as the solvent in its systems. The polymers and film-forming agents must be water-soluble or water-swellable respectively. (Zerbe; Col. 4, lines 4-5 and Col. 4, lines 59-61). Additionally, Zerbe specifically requires that the "solvents must be acceptable for food, food service, cosmetic and pharmaceutical products." (Zerbe; Col. 4, lines 4-5). Not only does Strobush teach away from applying its apparatus to water-based compositions, but to extract only the bottom drying disclosure therefrom while ignoring the remainder of its requirements, e.g., slow, incremental drying, and apply it to the water-based film compositions of Zerbe would destroy the intent and purpose of Strobush. *See In re Gordon*, 733 F.2d 900, 902, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984). As such, one of ordinary skill in the art would have no motivation to combine the teachings of Strobush with Zerbe in attempt to arrive at the presently claimed invention.

4. <u>No Reasonable Expectation of Success</u>

As provided in MPEP §2143, to establish a *prima facie* case of obviousness, there also must be "a reasonable expectation of success."

Not only is there no suggestion to combine the teachings of Zerbe, Strobush and Yuhki, as discussed above, there is no reasonable expectation of success that the hypothetical combination would work. As set forth above, Zerbe and Strobush relate to completely different chemical systems, which involve different processing considerations. Zerbe uses a conventional hot air oven to remove water from its edible film products. Strobush meanwhile teaches a complex drying apparatus, in which a number of sequential drying zones are employed to slowly remove highly volatile organic solvents. The entire objective of Strobush is to reduce mottle, i.e., surface defects in its coated substrates, which is a significant problem in Strobush's systems, as discussed above. There is no indication in Zerbe that mottle is a problem in its edible film products. Therefore, not only are the compositional make-up of the systems disclosed in Zerbe and Strobush disparate, but the problems experienced in forming such products are entirely

different. Based on such teachings, one skilled in the art would have no reason to expect that the drying apparatus taught in Strobush for reducing mottle in highly volatile organic solvent-based image coatings could be applied to Zerbe's aqueous-based edible compositions to produce dried, edible films suitable for human consumption. *See In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991) (explaining that "the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure").

Further, use of the Zerbe aqueous-based compositions with the Strobush teachings would not be expected to produce self-supporting, edible films, as produced in the present invention. That is, the amount of Active in each dose would not be expected to be predictable and compositional uniformity would not be expected to be obtained. (App. 1; Rounds Declaration, ¶ 27).

Therefore, there is no reasonable expectation of success that the apparatus involving sequential drying taught in Strobush for slow removal of volatile organic solvents could be used with Zerbe's compositions to produce dried films without destroying the active, e.g., flavor, contained therein. Moreover, there is no reasonable expectation of success that such hypothetical combination could produce an edible film having a uniform distribution of components throughout such that it could be divided into individual dosage units having the same amount of Active in each unit, as recited in Appellants' claims. Because there is no reasonable expectation of success based on the hypothetical combination of references, no *prima facie* showing of obviousness has been made.

5. **Hypothetical Combination of Zerbe, Strobush and Yuhki Fails to Yield All of the Limitations of the Claims**

Even assuming *arguendo* that Strobush is found to be analogous art and the combination of references is proper, the hypothetical combination of Zerbe, Strobush and Yuhki still does not result in all of the specific limitations of the claims. According to MPEP §2143.03, "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught

or suggested by the prior art." It is the Examiner's obligation to find all of the claim limitations in the prior art.

For example, the hypothetical combination of Zerbe, Strobush and Yuhki fails to yield a number of the claim limitations of claim 117. Specifically, the process of claim 117 requires a number of specific preliminary steps prior to drying the film, including: (1) forming a masterbatch premix of a water-soluble polymer and water; (2) deaerating the premix; (3) feeding a predetermined amount of the deaerated premix to at least one mixer; and (4) adding an active to the at least one mixer. Thereafter, the components are mixed to form a uniform distribution, the film is formed, fed onto a substrate and then dried. There is no disclosure or suggestion of this combination of four preliminary steps recited above in Zerbe, Strobush or Yuhki. The combination of steps comes only from applicant's disclosure.

Therefore, the proposed hypothetical combination fails to yield all of the claim limitations of Appellants' claim 117. The rejection of claim 117 based on this combination also should be withdrawn on this ground.

B. <u>CLAIMS 94 AND 95 ARE PATENTABLE OVER ZERBE IN VIEW OF STROBUSH, YUHKI AND HORSTMANN</u>

The Examiner has rejected claims 94 and 95 under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and Horstmann. Claims 94 and 95 are dependent on claim 91 and add a further limitation with regard to the wet film thickness. In the final Office Action dated January 20, 2006, the Examiner admitted that Zerbe fails to disclose films having thickness of at least 30μm or at least 500μm. The Examiner relied on Horstmann for allegedly disclosing edible films having a thickness of 0.003 to 4 mm. According to the Examiner, it would have been obvious to one skilled in the art to prepare an edible film having a thickness of 0.003 to 4 mm, as disclosed in Horstmann, according to the method of Zerbe as modified by both Strobush and Yuhki to provide a film having strength and texture. (Office Action, at page 8).

1. **No Motivation to Modify Strobush to Dry the Thick Aqueous-Based Films of Claim 95**

At the outset, claim 95 requires a wet film thickness of at least about 500μm. This claim is directed to thick, aqueous-based films. Such films are difficult to dry as the water must be driven off without causing all of the problems discussed above, such as surface skinning, aggregations and conglomerations of active particles, among others. Such thickness is well outside the range of wet coating thickness disclosed in Strobush. Specifically, Strobush discloses a wet coating thickness of about 100μm (Example 1 in Strobush is about 100μm based on the combination of the 81.3μm and 19.1μm wet layers; Example 2 in Strobush is about 108μm based on the combination of the 91.4μm and 17μm layers). In addition to being aqueous-based, the wet film systems recited in Appellants' claim 95 are about 5 times thicker than Strobush's coatings. Moreover, Appellants' claimed thickness range is well outside the typical arena of photographic image coatings. Accordingly, there would be no motivation for one skilled in the art to use Strobush's slow and incremental drying apparatus to attempt to dry such thick, aqueous-based films.

2. **Horstmann Does Not Suggest Drying From the Bottom**

Further, with respect to claims 94 and 95, as noted above, Horstmann was merely cited for its disclosure of film thickness. Horstmann is concerned with producing sheet like films, but does not suggest drying from the bottom or the rapid formation of a viscoelastic film. Indeed, Horstmann does not elaborate on the drying process other than to advise that the drying times are almost double the rapid drying times used by Appellant (4-6 min, Application, pp. 28, 32 versus 10-15 min, Horstmann, Exs. 1 and 3). Accordingly, Horstmann does not overcome the deficiencies noted above with respect to Zerbe, Strobush and Yuhki.

In view thereof, and because claims 94 and 95 depend from claim 91, it is respectfully submitted that these claims also are patentable.

C. CLAIM 96 IS PATENTABLE OVER ZERBE IN VIEW OF STROBUSH, YUHKI AND WITTWER

The Examiner has rejected claim 96 under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and Wittwer. The Examiner admitted that Zerbe fails to disclose films having a viscosity of about 400 cps to about 100,000 cps, as recited in claim 96. The Examiner relied on Wittwer for allegedly disclosing edible films having a viscosity of 2,000 to 2,500 cps. The Examiner asserted that it would have been obvious to one skilled in the art to "provide the matrix with a viscosity of 2,000 to 2,500 cps as disclosed by Wittwer in the method of Zerbe et al '292 as modified by combination of references to provide a material suitable for high speed commercial application." (Office Action, at pages 8-9).

Wittwer was merely cited for its disclosure of polymer matrix viscosity. There does not appear to be any disclosure of relevance to a process of forming and drying edible films having compositional uniformity. Accordingly, Wittwer cannot overcome the deficiencies noted above with respect to Zerbe, Strobush and Yuhki. Because claim 96 depends from claim 91, it is respectfully submitted that this claim also is patentable.

D. CLAIMS 98, 99, 102 AND 103 ARE PATENTABLE OVER ZERBE IN VIEW OF STROBUSH, YUHKI AND ZERBE '957

The Examiner has rejected claims 98, 99, 102 and 103 under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and Zerbe '957. The Examiner acknowledged that Zerbe fails to disclose the steps of dividing the film into dosage forms having equal dimensions, mass and thickness and packaging each individual dosage form, as recited in claims 98, 99, 102 and 103. The Examiner relied on Zerbe '957 for allegedly disclosing the steps of cutting the film into pieces and packing the dosages. According to the Examiner, it would have been obvious to one of ordinary skill in the art to combine the teachings of Zerbe '957 with Zerbe, Strobush and Yuhki to "cut the film into pieces of a shape and size that meet the requirement of intended application and packing the films or dosage into containers . . . to

provide an easy-to-use, cheap and reproducible flavoring or intermediates." (Office Action, at page 9).

Zerbe '957 was merely cited for its disclosure relating to cutting film into pieces and packaging the film into containers. Zerbe '957 contains no disclosure of any relevance to edible films having compositional uniformity, nor processes for achieving such films. Therefore, Zerbe '957 does not overcome the deficiencies noted above with respect to Zerbe, Strobush and Yuhki. Because claims 98 and 99 depend from claim 91, and claims 102 and 103 depend from claim 101, it is respectfully submitted that these claims also are patentable.

E. CLAIMS 104 AND 110 ARE PATENTABLE OVER ZERBE IN VIEW OF STROBUSH, YUHKI AND HORSTMANN

The Examiner has rejected claims 104 and 110 under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and Horstmann. Claims 104 and 110 are independent process claims. Both claims require at least the same general process requirements as discussed above with respect to independent claims 91, 101, 106, 108, 111, 112, 114, 117 and 119. Therefore, Appellants' remarks above in response to the Examiner's rejection of those independent claims over Zerbe, Strobush and Yuhki similarly are relevant here. Without repeating these remarks in detail, Appellants' reiterate that Strobush is not analogous art, and thus, is not properly useable in formulating a rejection of the claims herein. Additionally, as discussed above, there is no suggestion or motivation to combine Strobush with Zerbe and Yuhki, as well as no reasonable expectation that such combination could be used to successfully produce dried, edible films, which contain an accurate amount of active therein suitable for human consumption. These arguments are similarly applicable to claims 104 and 110 and for the sake of brevity are not repeated herein.

Further, Horstmann was merely cited for its disclosure of film thickness. As discussed above, Horstmann does not suggest drying from the bottom or the rapid formation of a

viscoelastic film. Accordingly, Horstmann does not overcome the deficiencies of Zerbe, Strobush and Yuhki noted above.

In view thereof, it is respectfully submitted that claims 104 and 110 are patentable over the cited combination of references.

F. CLAIM 116 IS PATENTABLE OVER ZERBE IN VIEW OF STROBUSH, YUHKI AND MEHRA

The Examiner has rejected claim 116 under 35 U.S.C. §103(a) as being obvious over Zerbe in view of Strobush, Yuhki and Mehra. Claim 116 is an independent process claim. It requires at least the same general process requirements as discussed above with respect to independent claims 91, 101, 106, 108, 111, 112, 114, 117 and 119. As discussed in detail above with regard to those claims, Strobush is not analogous art, and thus, is not properly useable in formulating a rejection of the claims herein. In addition, there is no suggestion or motivation to combine Strobush with Zerbe and Yuhki, as well as no reasonable expectation that the hypothetical combination would work. These arguments are similarly applicable to claim 116 and for the sake of brevity are not repeated herein.

Further, Mehra was merely cited for its disclosure of anti-foaming agents. Mehra does not include any disclosure of relevance to a process of forming and drying edible films having compositional uniformity. Accordingly, Mehra does not overcome the deficiencies of Zerbe, Strobush and Yuhki noted above.

In view thereof, it is respectfully submitted that claim 116 is patentable over the cited combination of references.

In sum, Strobush is nonanalogous art and cannot properly be applied against Appellants' present claims. In addition, there is no motivation to combine Strobush with Zerbe and Yuhki, as well as no reasonable expectation that the proposed hypothetical combination would be

successful. Finally, even taking the proposed hypothetical combinations suggested by the Examiner, the claims are not disclosed, particularly claim 117. It is respectfully submitted that claims 91, 93-104, 106, 108-112, 114, 116, 117 and 119 are patentable.

8. CONCLUSION

Having set forth factual and legal basis which support the patentability of the claims on appeal, it is respectfully submitted that claims 91, 93-104, 106, 108-112, 114, 116, 117 and 119 are in condition for allowance. Accordingly, Appellants respectfully urge the Board to reverse the Examiner's rejections of the claims.

Respectfully submitted,

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9. CLAIMS APPENDIX

91. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) mixing an edible water-soluble polymer component, water and an active component to form an edible matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing;

(c) forming a wet film from said deaerated matrix;

(d) providing a surface having top and bottom sides;

(e) feeding said film onto said top side of said surface;

(f) rapidly forming a visco-elastic film by applying hot air currents to said bottom side of said surface with substantially no top air flow to prevent flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components; and

(g) drying said visco-elastic film to form a self-supporting edible film.

93. The process according to claim 91, wherein said active component is taste masked.

94. The process according to claim 91, wherein said wet film has a thickness of at least about $30\mu m$.

95. The process according to claim 91, wherein said wet film has a thickness of at least about $500\mu m$.

96. The process according to claim 91, wherein said wet film has a viscosity of about 400 cps to about 100,000 cps.

97. The process according to claim 91, further comprising the step of removing said self-supporting film from said surface.

98. The process according to claim 97, further comprising the step of dividing said self-supporting film into individual dosage forms of substantially equal dimensions.

99. The process according to claim 98, further comprising the step of packaging each of said individual dosage forms.

100. The process according to claim 91, wherein said self-supporting film is formed in conjunction with a removable backing.

101. A process for making a self-supporting, edible film dosage unit having a substantially uniform distribution of components comprising:

(a) providing a wet matrix having a uniform distribution of edible components, said components comprising a water-soluble polymer component, an active component and water to form an edible matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing to prevent cavitation of the matrix in a manner which pulls air into the matrix;

(c) forming a wet film from said deaerated wet matrix;

(d) rapidly forming a visco-elastic film by applying hot air currents to said film to prevent flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components;

(e) drying said visco-elastic film to form a self-supporting edible film; and

(f) dividing said self-supporting film into dosage forms of substantially equal dimensions, wherein each of said dosage forms is compositionally equal.

102. The process according to claim 101, wherein each of said dosage forms has substantially the same mass.

103. The process according to claim 101, wherein each of said dosage forms has substantially the same thickness.

104. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) providing a wet matrix having a uniform distribution of edible components, said components comprising a water-soluble polymer component, an active component selected from the group consisting of pharmaceutical actives, cosmetic actives and combinations thereof and water to form an edible matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing to prevent cavitation of the matrix, thereby reducing formation of air bubbles;

(c) forming a wet film from said deaerated wet matrix, said film having a top surface, a bottom surface and a depth between said top and bottom surfaces;

(d) rapidly forming a visco-elastic film by applying hot air currents to said film to prevent flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components; and

(e) drying said visco-elastic film to form a self-supporting edible film, said dried film having a uniform distribution of said polymer and said solvent components, a uniform weight and a uniform thickness.

106. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) providing a wet matrix having a uniform distribution of edible components, said components comprising a water-soluble polymer component, an active component and water to form an edible matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing;

(c) forming a wet film from said deaerated wet matrix within a time period before the active degrades, said film having a top surface, a bottom surface and a depth between said top and bottom surfaces;

(d) rapidly forming a visco-elastic film by applying hot air currents to said film to initiate drying of the depth of said film prior to forming a polymer skin on said top surface of said film and to prevent flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components; and

(e) drying said visco-elastic film to form a self-supporting edible film, said dried film having a uniform distribution of said polymer and said solvent components, a uniform weight and a uniform thickness.

108. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) providing a wet matrix having a uniform distribution of edible components, said components comprising a water-soluble polymer component, an active component and water to form an edible matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing to reduce formation of air bubbles;

(c) forming a wet edible film from said deaerated wet matrix, said film having a top surface and a bottom surface;

(d) rapidly forming a visco-elastic film by applying hot air currents to said film, wherein said air currents are applied to said bottom surface of said film at a velocity greater than to said top surface of said film to prevent flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components; and

(e) drying said visco-elastic film to form a self-supporting edible film.

109. The process according to claim 108, wherein said air currents applied to said top surface of said film are less than that which cause surface rippling or skinning prior to drying of the depth of said film.

110. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) providing a wet matrix having a uniform distribution of edible components, said components comprising a water-soluble polymer component, a pharmaceutical active component and water to form an edible matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing;

(c) forming a wet edible film from said deaerated wet matrix, said film having a top surface, a bottom surface and a depth of at least about 500μm between said top and bottom surfaces;

(d) rapidly forming a visco-elastic film by applying hot air currents to said film, wherein said air currents are less than that which cause surface rippling or skinning prior to drying of the depth of said film, to prevent flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components; and

(e) drying said visco-elastic film to form a self-supporting edible film.

111. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) providing a wet matrix having a uniform distribution of edible components, said components comprising a water-soluble polymer component, an active component and water to form an edible matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing;

(c) forming a wet edible film from said deaerated wet matrix, said film having a top surface, a bottom surface and a depth between said top and bottom surfaces; and

(d) rapidly forming a visco-elastic film by applying hot air currents to said film to prevent flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components; and

(e) drying said visco-elastic film, wherein said dried film is self-supporting and said top surface of said dried film is non-rippled.

112. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) combining and mixing an edible water-soluble polymer component, an active component and water to form an edible matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing to reduce air bubble inclusions and applying a vacuum;

(c) forming an edible film from said deaerated matrix, said film having a top surface and a bottom surface;

(d) drying said film from said bottom surface to said top surface by applying hot air currents to said bottom surface of said film until a visco-elastic film is achieved; and

(e) further drying said visco-elastic film to form a self-supporting edible film.

114. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) providing a wet matrix having a uniform distribution of edible components, said components comprising a water-soluble polymer component, an active component and water to form an edible matrix with a compositionally uniform distribution of components;

(b) deaerating said matrix by mixing;

(c) forming a wet edible film from said deaerated wet matrix, said film having a top surface, a bottom surface and a depth between said top and bottom surfaces;

(d) rapidly forming a visco-elastic film by applying hot air currents to said film, wherein said air currents are insufficient to cause one or more of the following:

(i) surface skinning prior to drying the depth of said film;

(ii) surface rippling;

(iii) self-aggregation of components;

(iv) non-uniformity in the thickness of said film; and

(v) non-uniformity of mass per unit volume; and

(e) drying said visco-elastic film to form a self-supporting edible film.

116. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) combining and mixing an edible water-soluble polymer component, an edible active component and water to form an edible matrix with a compositionally uniform distribution of components;

(b) adding an anti-foaming agent to release oxygen from said mixture of components;

(c) further deaerating said matrix by mixing;

(d) forming a wet edible film from said deaerated matrix;

(e) providing a surface having top and bottom sides;

(f) feeding said wet film onto said top side of said surface;

(g) rapidly forming a visco-elastic film by directing hot air currents at said bottom side of said surface to prevent air flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components; and

(h) drying said visco-elastic film to form a self-supporting edible film.

117. A process for making a self-supporting, edible film having a substantially uniform distribution of components comprising:

(a) forming a masterbatch premix of an edible water-soluble polymer component and water;

(b) deaerating said premix by mixing;

(c) feeding a predetermined amount of said deaerated premix to at least one mixer;

(d) adding an active component to said at least one mixer;

(e) mixing said active component and said predetermined amount of said premix to form a matrix having a uniform distribution of components;

(f) forming a wet film from said matrix;

(g) providing a surface having top and bottom sides;

(h) feeding said film onto said top side of said surface;

(i) rapidly forming a visco-elastic film by applying hot air currents to said bottom side of said surface with substantially no top air flow to prevent air flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components;

(j) drying said visco-elastic film to form a self-supporting edible film; and

(k) removing said self-supporting film from said surface.

119. A process for making a film having a substantially uniform distribution of components comprising:

(a) combining a water-soluble polymer component, an active component and water to form a matrix with a compositionally uniform distribution of said components;

(b) deaerating said matrix by mixing;

(c) forming a film from said deaerated matrix;

(d) providing a surface having top and bottom sides;

(e) feeding said film onto said top side of said surface;

(f) rapidly forming a visco-elastic film by applying heat to said bottom side of said surface to prevent air flow migration and intermolecular forces from creating aggregates or conglomerates thereby maintaining the compositional uniform distribution of components; and

(g) drying said visco-elastic film to form a self-supporting edible film.

10. EVIDENCE APPENDIX

A copy of the Declaration Under 37 C.F.R. §1.132 by Dr. Rhyta Rounds submitted with Appellants' Response dated May 9, 2006 is attached hereto at Appendix 1. In the Advisory Action dated May 22, 2006, the Examiner indicated that this declaration was entered in the record.

11. RELATED PROCEEDINGS APPENDIX

No related appeals or interferences are known to Appellants or Appellants' legal representative which will directly affect or be directly affected by or have bearing on the Board's decision in this appeal.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	R. K. Yang et al.	Examiner:	Chan, Sing P.
Application No.:	10/074,272	Group Art Unit:	1734
Confirmation No:	4926	Docket:	1199-4 RCE
Filed:	February 14, 2002	Dated:	May 9, 2006
For:	THIN FILM WITH NON-SELF-AGGREGATING UNIFORM HETERO-GENEITY AND DRUG DELIVERY SYSTEMS MADE THEREFROM		

Commissioner for Patents
P.O. Box 1450,
Alexandria, VA 22313

I hereby certify this correspondence is being deposited with the United States Postal Service as first class mail, postpaid in an envelope, addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313
On: May 9, 2006
Signature: /K.J. Goodhand/ K J Goodhand

DECLARATION BY RHYTA S. ROUNDS, Ph.D. UNDER 37 C.F.R. §1.132

Sir:

I, Rhyta S. Rounds Ph.D., do hereby make the following declaration:

I. Technical Background

1. Attached as Exhibit A is a copy of my curriculum vitae. As noted therein, I have worked in the field of material science, particularly experimental rheology, for 30 years.

2. My work experience includes 11 years as the Research Director of Fluid Dynamics, Inc., 2 years of employment with Becton Dickinson Vacutainer Systems, 9 years of

employment with Colgate-Palmolive Company and 1 year of employment with CPC Americas. During these periods of employment, I worked extensively with the rheology of various fluid systems, including the processing of complex fluids. I have worked on structured fluid systems for application to the pharmaceutical, food, cosmetic/toiletries and coatings and adhesives industries.

3. During my career, I was an inventor on numerous patents directed to complex fluid systems. I have direct experience with fluid systems which produce mottle, as well as an understanding of the uniform distribution of active/unit volume of the present invention.

4. I have been hired as a consultant by MonoSolRx, LLC (the assignee of the above-identified application) to provide an expert analysis on an issue related to the prosecution of U.S. Application No. 10/074,272 (hereinafter the "Invention" or "Present Application"). While I am being paid for my services, I am not an employee of MonoSolRx, LLC nor do I have any financial interest in MonoSolRx, LLC.

5. I have reviewed a copy of U.S. Patent No. 5,881,476 to Strobush et al. (hereinafter "Strobush") and the January 20, 2006 Office Action issued with respect to the subject application. I also have reviewed the Present Application. I have been requested to provide my opinion as to the technical distinctions between mottle and compositional uniformity as they are each defined in Strobush and the Present Application, respectively. I have also been requested to provide an analysis as to applicability of the Strobush teachings to water-based processes to make water-soluble film with a uniform distribution of active/unit volume.

6. In the Office Acton, the Examiner equates mottle with compositional uniformity. "Mottle" as defined in Strobush is a technical problem different from "Compositional Uniformity" as defined in the Present Application.

II. <u>Strobush and the Present Application Relate to Entirely Different Technologies</u>

7. To begin with, Strobush relates to technology which is in an entirely different field than the Present Application. Strobush is directed to non-ingestible coated substrates used

in the manufacture of imaging articles. The coatings applied to the substrate are non-aqueous, particularly alcohol/ketone-based, colloidal emulsions. Such systems are highly volatile and typically have low viscosities.

8. In contrast, the Present Application is directed to ingestible films for the oral delivery of actives, particularly pharmaceutical actives. The films of the Present Application are aqueous systems, which include dispersions of relatively large active particles in a viscous water-based matrix. The Present Application forms a highly viscoelastic matrix.

III. Definition of Mottle

9. Strobush teaches a process and apparatus for producing thin, mottle-free photothermographic, thermographic and photographic coatings on a substrate. A complex drying apparatus is described in detail with a plurality of zones expressly designed to control and eliminate mottling. A definition of what is meant by mottle is provided in column 1, lines 59-67 and column 2, lines 1-5:

> **Mottle is an irregular pattern or non-uniform density defect that appears blotchy when viewed. This blotchiness can be gross or subtle. The pattern may even take on an orientation in one direction. The scale can be quite small or quite large and may be on the order of centimeters. Blotches may appear to be different colors or shades of color. In black-and-white imaging materials, blotches are generally shades of gray and may not be apparent in unprocessed articles but become apparent upon development.**

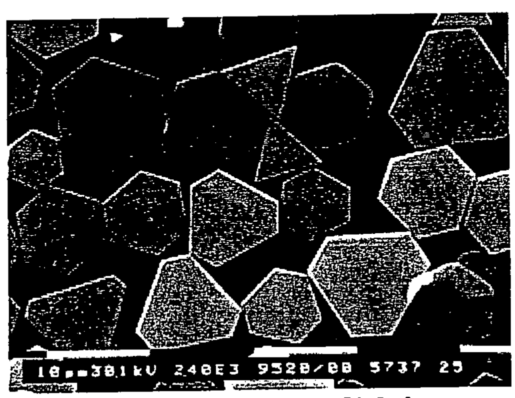
10. In short, mottle, in the context of Strobush, relates to visually observable surface defects on a substrate coating. Mottle is further described by Strobush in column 2, lines 6-19, as being "an undesirable defect because it detracts from the appearance of the finished product."

11. Mottle is repeatedly stated as the problem being addressed in Strobush, and in fact, it is the sole problem addressed by Strobush. For example, see SUMMARY OF THE INVENTION, column 6, lines 24-29, where it is expressly stated that drying coated substrates can be accomplished "...without introducing significant mottle..." The disclosure is replete with

express statements regarding the invention's purpose of "minimizing the formation of mottle". Exhibit B, attached hereto, sets forth 28 passages in Strobush where the problem to be overcome is expressly stated as reducing mottle.

12. Mottle is a serious problem for Strobush because Strobush's emulsion system is largely composed of highly volatile organic solvents, such as 2-butanone (methyl ethyl ketone or MEK), in which many of the emulsion ingredients are dissolved. *See* Strobush, Col. 2, lines 16-19.

13. The coatings used in Strobush are extremely thin and could not function independent of a permanent substrate. Film coatings in the liquid phase are cited in Strobush as being sub-millimeter (<10 mil), which is extremely thin (on the order of microns). *See* Strobush Examples 1 and 2 (wet emulsion layers are 81.3 microns and 91.4 microns, respectively). Strobush's thin coatings are not capable of being self-supporting films. They are designed to be part of a laminate or multi-layer structure, with the substrate being integral with and inseparable from the coating, such as in a photograph. The emulsion layer, as defined in Strobush (Column 7), contains a photosensitive silver halide or reducible silver source. Silver halide is a photoactive microcrystalline solid, as shown in the photomicrograph below:



Electron micrograph of tabular grain emulsion

(from Kodak)

14. Silver particles useful in such emulsion coatings are microscopic and are understood to those skilled in the art to be one (1) micron or less. *See* R.J. Stokes et al.,

Fundamentals of Interfacial Engineering, 120 (1997). The silver behenate core/shell particles actually used in Strobush have an average grain size of 0.04-0.05 μm. *See* U.S. Patent No. 5,382,504, Col. 23-24 (cited in Strobush at Col. 18, lines 40-41). The silver particles must be aligned properly on the substrate surface in order to prevent imperfections, i.e., mottle, in the appearance of the photo- or thermo-developed image. These small particles are highly energetic surfaces, with high surface areas. Consequently, as a colloid, interfacial forces and physical chemistry govern their behavior. With appropriate particle surface treatments, steric stabilization and Brownian motion maintain sol physical stability.

15. Strobush addresses the problem of mottle in its coatings using a complex drying apparatus, which includes a sequence of zones. In Strobush, the multi-zoned and sub-zoned apparatus is critical to minimizing or reducing defects in coating appearance, which would blur or otherwise detract from the image produced by the coating. Strobush's apparatus and process controls the colloid and surface properties of its solvent based emulsion and other layers by controlling the heat transfer rate and temperature difference between the temperature of the drying gas and the temperature of the coated substrate, i.e., emulsion layer laminated to the underlying photographic paper or other substrate.

16. To obtain a photo- or thermo-graphic image which is not blurred or blotched, Strobush dries his very thin coatings in an elaborate sequence of zones in order to control the evaporation rate of volatile, non-aqueous solvent and prevent disruption or the preferential alignment of the sub-micron sized silver particles. By doing so, Strobush reduces or minimizes mottle.

17. In summary, the problem of mottle in Strobush involves a blurred or blotchy coating, which is undesirable in a photographic coating.

IV. <u>Definition of Compositional Uniformity</u>

18. Compositional uniformity as expressed in the Present Application means that during processing, the composition must maintain uniformity in content of all components such that the product formed contains the same amount of active throughout (within acceptable

regulatory variances), as well as a uniform product thickness ("Compositional Uniformity"). *See* U.S. Application No. 10/074,272, ¶ [0010]. This is critical for drug-containing films in order to provide safe and effective consumer products and thereby satisfy FDA-approval requirements. Stringent government controls in the production of pharmaceutical products are mandated by federal law and without uniform active content, such products cannot be legally used or sold. For example, a 250μm thick x 1" x ½" piece of dry film, cut from one region of a manufactured roll, must contain the same components in substantially the same relative amounts as an equally-sized piece of film cut from another region of the manufactured roll.

19. To achieve this, a flowable wet film-forming composition containing ingestible active dispersed or dissolved in a non-toxic liquid, e.g., water, must first be formed which can be laid down onto a drying surface as a uniform composition. Mixing of the components to form the composition must be done thoroughly and in a manner to ensure uniformity, particularly of the active, and to prevent excess air from being pulled into the mixture. Excess air produces random voids within the film during drying, which can destroy Compositional Uniformity.

20. Once the uniform wet film composition is laid onto a drying surface, the water component must by evaporated and the film must be dried through a process that prevents the dispersed phase containing the active from migrating or aggregating. This problem is solved by quickly maintaining and further enhancing the viscoelastic state such that uniformity of the components in the film is "locked in." This is accomplished by bottom drying, without disturbing the physical thickness of the film by excessive top air flow. The combination of steps of the Present Application prevent migration or aggregation of the dispersed phase, prevent surface skinning and re-rupture as water evaporates, and minimize trapped air voids, which would otherwise be present if surface skinning occurred. The result is a self-supporting film product that can be divided into dosage units and safely ingested due to its Compositional Uniformity.

V. <u>Mottle is a Different Technical Problem than Compositional Uniformity</u>

21. In the Office Action, the Examiner equates the problem of mottle with the Present Application's problem of Compositional Uniformity. *See* Office Action, at page 6. Mottle,

however, is a different technical problem than achieving Compositional Uniformity throughout a film, particularly as the films of the Present Application are distinctly different from the coatings taught by Strobush and require different processing considerations.

22. As seen above, solving the problem of mottle in an emulsion system based on highly volatile solvents, as taught in Strobush, does not address in any way the problem of Compositional Uniformity in a drug delivery system based on aqueous dispersions of particles.

23. The problem addressed in the Present Application is finding a process for obtaining bulk Compositional Uniformity throughout a self-supporting oral dosage film strip. The Present Application seeks to make relatively thick, self-supporting films, which do not require a backing or laminate structure to perform their function. Wet film thickness is on the order of 500-1,500 μm (micron). *See* U.S. Application no. 10/074,272, at ¶ [0091]. The product produced from the inventive process is an oral dosage film strip for delivery of an active, such as a flavor or drug, to a consumer.

24. Contrary to the very thin colloidal photographic coatings made by Strobush, when particles of actives are present in the inventive films, they are significantly larger, e.g., drug particles are typically 50 microns or greater, more specifically about 50 to 250 microns. Further, these particles are typically irregular in size and shape and are present in a distribution of particle sizes, unlike silver halide, for example. The problem of creating a self-supporting film product that includes such large particles and that has Compositional Uniformity is entirely different from the problem of producing a mottle-free photographic emulsion coating.

25. The relatively large suspended particles, such as drug particles, in the films of the Present Application, behave very differently than the small colloidal particles of Strobush's coatings. Large particle dispersions, such as in the Present Application, typically migrate, fall out of solution and/or aggregate. Colloidal emulsions, such as in Strobush, do not experience such problems. For example, milk is a colloidal emulsion. Milk retains its suspension without experiencing separation problems. This is typical of colloidal emulsions. Large particle dispersions present completely different technical challenges and problems than small colloidal

systems, such as shown in Strobush. Brownian motion, long range attractive and repulsive forces, for example, are significant factors in colloid systems; external forces, such as gravity, are far more important in large particle dispersed systems. Obtaining a dried, relatively thick film with the proper amount of active distributed throughout is unrelated to the surface appearance, and in fact surface imperfections in the inventive films are expected. Large particles adjacent the film surface may create a rough appearance or sandpaper-like effect. Such surface imperfections are entirely acceptable and in fact expected in the Invention.

26. In fact, Strobush itself recognizes that mottle is a different problem from other surface defects in aqueous systems. In particular, mottle, according to Strobush, is a different problem than surface bubbles and blistering formed when aqueous, latex paint dries. At Column 4, lines 6-9, Strobush states that the "formation of mottle occurs due to a different mechanism than blisters and requires a different method for control and elimination." Thus, even among other surface defects formed by drying coatings, mottle is seen by Strobush as a different problem.

VI. The Strobush Process has Numerous Contrary Teachings and Characteristics to the Invention and Water-Based Processes

27. A careful reading of Strobush indicates its contrary teachings from the Present Application. Tabulated below are examples of some of the process characteristics that play a role in each of the Present Application and in Strobush. As the table indicates, the differences are cogent reminders of different considerations and goals of the two processes.

Inventive Process Characteristics	Strobush Process Characteristics
Edible film	Photographic coating
Water	MEK (highly volatile toxic organic solvents)
Viscoelastic matrix	Low viscosity (rheology not mentioned)
Active (e.g., temperature-, oxidative- and/or hydrolytically-sensitive)	No ingestible actives
Relatively large particles (macro-suspension)	Nanoparticles (colloidal dispersion)
Self supporting doses	Permanent thin coating on a substrate
Rapid heating to create large temperature differential	Very small temperature differential in a plurality of heating zones
Benard cells	No Benard cells
De-aeration	De-aeration not possible
Compositional uniformity (mass of active/unit volume)	Mottle free (perfect surface)
Surface imperfections generated (mottle is acceptable)	No surface imperfections

28. In view of these stark differences, one skilled in the art would not consider Strobush relevant or applicable to water-based, edible systems, and would not be inclined to consult Strobush to solve drying problems associated with water-based edible films.

29. One of ordinary skill in the art with respect to processes for making edible active-containing products, would not arrive at the Present Application from the teachings of Strobush. In fact, use of the Strobush process with the compositions of Zerbe would not be expected to produce the products of the Invention.

VII. <u>Compositional Uniformity in Drug Products and the Process of Making Uniform Drug Products is Governed by FDA Requirements</u>

30. Compositional Uniformity is vital for oral film delivery strips to provide safe and effective consumer products. Without Compositional Uniformity, individual film products containing drug cannot achieve FDA approval for consumer use and essentially have no value. The surface appearance of such film products is of no consequence to their consumer safety and efficacy and the FDA approval process, and thus, mottle is irrelevant to solving this problem.

VIII. Conclusion

31. The process of Strobush involves producing extremely thin photographic coatings by incrementally ramping up the temperature to avoid disalignment of silver particles in a solvent-based emulsion, which otherwise results in a defective image, i.e., mottle. The end-product is a photoactive coating on a substrate used to produce images. In contrast, the inventive process is directed to achieving self-supporting oral film strips for delivery of actives by controlling and "locking in" the physical properties of the composition during the drying process, such that uniformity in the composition is maintained. The final product is an active-containing strip for safe and efficacious delivery to a consumer. Strobush's process of producing a photographic coated substrate is not technically germane to the production of an oral dosage film strip having Compositional Uniformity.

32. Therefore, mottle as taught by Strobush is an entirely different problem from Compositional Uniformity throughout a film. Moreover, the two different technical problems are addressed using two different processes to achieve entirely different products.

33. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Dated this 9th day of May, 2006

Rhyta S. Rounds Ph.D.

EXHIBIT A

Rhyta Sabina Rounds
68 Sand Hill Road
Flemington, New Jersey 08822
(908) 303-4920

SUMMARY OF QUALIFICATIONS:

More than thirty years of progressive industrial experience in material science. Emphasis has been in experimental rheology, in support of product/process development and manufacturing. Hold advanced degrees in Chemical Engineering.

PROFESSIONAL EXPERIENCE

Fluid Dynamics, Inc
45 River Road
Flemington, NJ 08822

Research Director 1995-present

Organized independent commercial rheology laboratory focused on complex fluid technology. Primary objective of this laboratory is two-fold : worldwide rheology testing and basic research in structured fluid systems for application to the pharmaceutical, foods, cosmetic/toiletries, coatings and adhesives industries as well as the design/manufacture of rheology testing instrumentation.

Becton Dickinson Vacutainer Systems 1993-1995
1 Becton Drive
Franklin Lakes, New Jersey

Research Fellow 1994-1995

Responsible for development of next generation serum/plasma separation medical devices having improved compatibility with diverse diagnostic immunoassays.

Senior Manager 1993-1994

Directed R&D Worldwide Technical Support in specimen separation blood collection medical devices. Manager of Materials Technology and Analytical Sciences groups. Responsible for maintenance and revitalization of product line accounting for 80% of division profitability.

Managed staff of eight with operating/project budget in excess of $1.5MM.

Worldwide team leader for collaborative research programs for improved immunoassay diagnostics.

- Developed interactive R&D/Marketing/Sales/Customer Service team for rapid response to customer complaints in serum/plasma blood collection tubes.
- Coordinated joint supplier/R&D teams for increased quality of incoming raw materials and revised

specifications.

- Developed strategic alliances facilitating the development of next generation products.
- Identified manufacturing/raw material cost reductions in excess of $1.75MM/yr.
- Implemented new production quality control measures increasing QC reliability and efficiency.
- Identified new gel chemistries for plasma/serum separation providing performance/cost advantage.
- Responsible for development of Gel Technology Center of Excellence.

Colgate-Palmolive Company 1984-1993
Technology Center
Piscataway, New Jersey

Senior Technical Associate 1991-1993

Worldwide Fabric Care Process Team Leader in Manufacturing Engineering Technology group. Responsible for process development/implementation for new liquid detergent products and optimization of existing production lines.

Managed staff of three with project activities in North America and the Far East with primary emphasis in Mexico, Malaysia and Australia.

- Developed core competency in rheology and the processing of complex fluids and surfactant systems.
- Identified process methods for liquid detergents resulting in cost savings of $32M/yr and capital cost avoidance in excess of $75M per production line.
- Identified accurate scale-up procedures for high volume-fraction liquid detergent dispersions from 1 liter to 20 metric ton plant scale operations.
- Revised raw material specifications worldwide for increased quality control and improved product performance.

Research Associate 1988-1990
Senior Research Engineer 1986-1988
Research Engineer 1984-1986

Managed rheology research group of three with department budget of $340M.

- Established new R&D department with mission to develop core competency in stable complex fluids with strong skill base in rheology, material science and surfactant/physical chemistry.
- Developed state-of-the-art rheology lab supplemented with electrical property measurements and extensive data acquisition expertise.
- Developed next generation gel liquid dishwasher detergent with improved product stability and performance with market introduction FY89. Product evaluated by Consumer Reports to be the Best New Liquid Detergent in 1990.
- Coordinated external/internal research programs for product quality improvements in Oral Care, Fabric Care, Household Surface Care and Advanced Research groups.
- Identified alternative applications for detergent systems in energy storage devices resulting in licensing proposals for the new technology.

CPC Americas 1977-1978
Best Foods Division
Commerce Street
Union, New Jersey

Process Development Engineer

- Conducted pilot plant research leading to full-scale production.
- Start-up team member for vegetable oil hydrogenation processes.
- Evaluated catalysts for hydrogenation.
- Modeled sterilization processes for process control.

EDUCATION

Stevens Institute of Technology
Hoboken, New Jersey
Department of Chemical Engineering

Post-Doctoral Research Fellow
Research Topic: Enhanced Membrane Separation Processes Coupled with Rapid-Pressure Swing Adsorption
1983-1984

Ph.D., Chemical Engineering
Thesis: Dielectrically Enhanced Permeability of Glassy Polymer Films
Graduation: 1982

Masters of Engineering, Chemical Engineering
Thesis: Anisotropic Thermal Conductivity of Oriented PET Films
Graduation: 1980

Completed Undergraduate Curriculum in Chemical Engineering
1975-1977

Rutgers University
Newark Campus
Newark, New Jersey

Bachelor of Arts, Geography
Graduation: 1973

Patents

US Patent, 6,149,821: Balanced Water Purification System.

US Patent 6,120,698: Balanced Water Purification System.

US Patent 5,807,970: Blood compatible, shear sensitive formulations.

US Patent 5,663,285: Blood compatible, shear sensitive formulations.

US Patent 5,427,707: Thixotropic aqueous compositions containing adipic or azelaic acid stabilizer.

US Patent 5,525,241: Linear viscoelastic aqueous liquid automatic dishwasher detergent composition.

US Patent 5,245,512: Nonisotropic solution polarizable material and electrical components produced therefrom.

US Patent 5,232,621: Linear viscoelastic gel compositions.

US Patent 5,064,553: Linear-viscoelastic liquid automatic dishwasher detergent composition.

US Patent 5,053,158: Linear-viscoelastic liquid automatic dishwasher detergent composition.

US Patent 5,038,249: Nonisotropic solution polarizable material and electrical components produced therefrom.

US Patent 4,974,118: Nonisotropic solution polarizable material and electrical components produced therefrom.

US Patent 5,206,797: Nonisotropic solutions polarizable material and electrical components produced therefrom.

US Patent 4,878,150: Polarizable material having a liquid crystal microstructure and electrical components produced therefrom.

Presentations and Publications

2nd Edition in preparation. Liquid Detergents, Surfactant Science Series, Volume 67. Ed, K-Y Lai, Chapter 4, "Rheology of Liquid Detergent Systems", Marcel Dekker, 1997.

2nd Edition in preparation. Liquid Detergents, Surfactant Science Series, Volume 67. Ed, K-Y Lai, Chapter 14, "Processing of Liquid Detergents: A Manufacturing Overview", Marcel Dekker, 1997.

Rheology of reactive polymer systems. R. S. Rounds, ACS National Meeting, Application Rheology of Dispersed Systems, Boston, August 18, 2002.

ACS National Meetings, R S Rounds, Presiding: Application Rheology of Dispersed Systems, Boston, August 18, 2002.

Evaluation of the Rheological Properties of Sulfonic Acids and Sodium Sulfonates, Berna, J.L., Bergoechea, C., Moreno, A., Rounds, R.S. Journal of Surfactants and Detergents, 3,3,Jjuly 2000).

Sulphonic acids and sodium sulfonates. Rheological properties and phase behaviour. C. Bengoechea, A. Moreno, J. L. Berna, Petresa, Spain R.S. Rounds, Fluid Dynamics, USA. M. Caffrey, Ohio State University, USA, Personal Care Ingredients Asia, November, 1999.

Rheological Characterization of an Aluminum Nitride Nanoparticle Suspension in Poly(Amic Acid)-NMP System, Mater. Res. Soc. Symp Proc. 501, Feb. 1998; with X. Chen and R. S. Rounds.

Powder Coating Institute Meeting, 1996, Cincinnati. Test Methods Development Sub-Committee, Invited Speaker. *Rheological Measurement of Curing Powder Coatings.*

Liquid Detergents, Surfactant Science Series, Volume 67. Ed, K-Y Lai, Chapter 4, "Rheology of Liquid Detergent Systems", Marcel Dekker, 1997.

Liquid Detergents, Surfactant Science Series, Volume 67. Ed, K-Y Lai, Chapter 14Processing of Liquid Detergents: A Manufacturing Overview", Marcel Dekker, 1997.

HBA "96 Educational Conference, New York. Invited Speaker. *Model Systems for Testing Product Concepts: Setting Effective Guidelines for Product Development.*

Society of Cosmetics Chemists, 1995, New York. Key Note Speaker: *Product Development & The Product Delivery Vehicle.*

Bath Gels: Rheology and Consumer Perceptions. Cosmetics & Toiletries. April, 1995.

ACS National Meeting, 1993, Chicago. Session Chairperson: Polymers in Aqueous Media.

ACS National Meeting, 1993, Chicago. Short Course Lecturer: Polymeric Hydrophilic Gels.

Shear Induced Phase Transitions of Anionic Surfactant Pairs, ACS National Meeting, 1993, Chicago. Symposium: Rheology of Surfactant Solutions. Invited Speaker.

Shear Effects in Surfactant Solutions, ACS Symposium Series 578, eds. C Herb, R Prud'homme, ACS, 1994.

Hydration Kinetics of Water Soluble Polymers, Society of Rheology Meeting, 1990, Santa Fe.

Physical Stability of Concentrated Dispersions, AIChE Annual Meeting, 1992, Miami.

A New Supercapacitor as a Replacement of Rechargeable Batteries, Third International Rechargeable Battery Seminar, 1990, Florida.

Surfactants in Electric Double Layer Capacitors: Use as Load Leveling Devices in Electric Vehicles, Ford Motor Company, Michigan, 1989.

Rheology of Aqueous Clay Dispersions, Princeton University, Chemical Engineering Seminar Series, 1988.

Enhanced Permeability of Polymer Films, ANTEC, 1983.

Dielectrically Enhanced Permeability of Polymer Films, Plastics Institute of America, Stevens Institute of Technology, 1981.

Anisotropic Thermal Conductivity of Oriented PET Films, ANTEC, 1978, New Orleans.

EXHIBIT B

Column 2, lines 6-19	Mottle is "an undesirable defect because it detracts from the appearance of the finished product."
Column 6, line 67-column 7, line 1	"...minimizing the formation of mottle as the coating solvent is evaporated."
Column 9, lines 13-14	"...minimizing the creation of drying defects, such as mottle."
Column 10, lines 5-6	"...mottle on the first and second coating edges is minimized."
Column 12, lines 27-28	"dried without introducing significant mottle defects..."
Column 12, lines 40-41	"The heat transfer rate is the coating 12 is the key to preventing or minimizing mottle formation."
Column 13, lines 30-31	"...without causing mottle..."
Column 13, line 38	"...to prevent mottle..."
Table I	"Maximum heat transfer rate without mottle formation -hΔT"
Column 13, line 66	"...mottle is not caused."

Column 14, lines 11-12	"...without causing mottle."
Column 14, line 24	"...while still avoiding mottle."
Column 14, lines 29-30	"...without formation of mottle."
Column 15, lines 29-30	"...formation of mottle is minimized or prevented."
Column 15, line 47	"...to minimize mottle formation..."
Column 19, line 49	"...dried to be mottle proof..."
Column 19, lines 58-60 and 64-66	"...severity of mottle was determined...amount of mottle was subjectively determined...films were visually inspected for mottle...mottle was rated as high, medium or low."
Column 20, line 3	"...level of mottle increased..."
Table 4	"Mottle Rating"
Column 20, line 21	"Drying more harshly increased the severity of the mottle."
Column 20, lines 37-41	"In order to determine the effect on mottle..."
Table 5	"Mottle Rating"

Column 20, lines 63 & 67	"...the severity of mottle increased."
Table 6	"Mottle Rating"
Column 21, line 22	"...the severity of mottle increased."
Table 7	"Mottle Rating"
Column 21, line 42	"...the severity of mottle increased."
Table 9	"Mottle Rating"

All claims are directed to a method or apparatus for evaporating a coating solvent from a coating on a surface of a substrate and "reducing mottle" as the solvent evaporates.